Applicants respectfully disagree with the statements at pages 2-3 of the Office Action that the elections were made without traverse. Applicants' response clearly stated that the elections were made with traverse and that there was no undue burden on the Examiner to search the subject matter of Groups I and II.

At pages 3-6 of the Office Action, claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86 and 100-101 have been rejected under 35 U.S.C. §103(a) as obvious over US 5,846,966 ("Rosenblum et al.") and The Medical Letter on Drugs and Therapeutics (1998) 40:1030: 68-69 ("Medical Letter"). Claims 21 and 32 were rejected under 35 U.S.C. §103(a) as obvious over Rosenblum et al. and the Medical Letter, further in view of Basic & Clinical Pharma., 6th Ed. (1995) 529 ("Katzung").

For brevity, the reasons for rejection are not repeated herein but reference is made to the outstanding Office Action.

Applicants respectfully traverse these rejections and request that the rejections be reconsidered and withdrawn.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24

U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

It is respectfully submitted that the combination of the references cited as rendering the claimed invention obvious is improper because there is no suggestion in the cited references to combine the claimed components of sterol absorption inhibitor (such as that of Formula (II) (e.g., ezetimibe)) and PPAR activator (such as fenofibrate).

Neither Rosenblum et al. nor Medical Letter provides motivation for substituting a PPAR activator for the statin used in combination with ezetimibe described in Rosenblum et al. As disclosed in the Medical Letter Clinical Study section at page 68, fenofibrate is not as effective as statins in lowering LDL cholesterol, a major risk factor in atherogenesis. Since statins are more effective in lowering LDL cholesterol, there is no motivation to substitute a PPAR activator such as fenofibrate for the statin in the combination disclosed in Rosenblum et al.

There is no guidance provided by Rosenblum et al. nor Medical Letter to pick and choose among numerous cholesterol treatments to select the particularly claimed combination of sterol absorption inhibitor (such as that of Formula (II) (e.g., ezetimibe)) and PPAR activator (such as fenofibrate).

With respect to claims 21 and 32, neither Rosenblum et al., Medical Letter nor Katzung, taken alone or together as suggested in the Office Action, provides any motivation for a triple combination treatment of sterol absorption inhibitor (such as that of Formula (II) (e.g., ezetimibe)), PPAR activator (such as fenofibrate) and niacin. These references provide no guidance or motivation as to the desirability for such as combination or selecting the particular components of the combination, or the potential effect of drug-drug interactions. For example, in the Drug Interaction section at page 69, Medical Letter discloses that it is unclear whether, like gemfibrozil and niacin, concurrent administration of fenofibrate with a statin could increase the risk of rhabdomyolysis. Katzung does not provide any motivation to combine a sterol absorption inhibitor (such as that of Formula (II) (e.g., ezetimibe)), PPAR activator (such as fenofibrate) and niacin.

Because of the difference of the way that each component of the presently claimed combination acts, it is respectfully submitted that the rejection is based upon an improper combination of references.

Accordingly, reconsideration and withdrawal of the §103(a) rejections is respectfully requested.

In view of the foregoing remarks, it is respectfully submitted that all of the pending claims in the present application are distinguishable from the cited prior art.

Accordingly, reconsideration and withdrawal of the rejections and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

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